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**CENTRAL FAX CENTER**  
**DEC - 9 2008**

Application No. 10/540,494  
Amendment dated December 9, 2008  
Reply to Office Action of August 11, 2008

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Docket No.: 63628(46342)

**AMENDMENTS TO THE SPECIFICATION**

Please replace the paragraph bridging pages 128 and 129 with the following amended paragraph:

Specifically, the substance that alters the binding property of metastin to the metastin receptor is screened by the following procedures. First, a receptor preparation is prepared by suspending a cell containing the metastin receptor or a membrane fraction of the cell in a buffer appropriate for use in the screening method. Any buffer can be used so long as it does not interfere the metastin-metastin receptor binding, including a phosphate buffer or a Tris-HCl buffer, having pH of 4 to 10 (preferably pH of 6 to 8), etc. For the purpose of minimizing non-specific binding, a surfactant such as CHAPS, Tween TWEEN-80<sup>TM</sup> (Kao-Atlas Inc.), digitonin, deoxycholate, etc., may optionally be added to the buffer. Further for the purpose of suppressing the degradation of the metastin receptor or metastin with a protease, a protease inhibitor such as PMSF, leupeptin, E-64 (manufactured by Peptide Institute, Inc.), pepstatin, etc. may also be added. A given amount (5,000 cpm to 500,000 cpm) of the labeled metastin is added to 0.01 ml to 10 ml of the receptor solution, in which  $10^{-4}$  M to  $10^{-1}$  M of a test compound is co-present. To determine the amount of non-specific binding (NSB), a reaction tube charged with unlabeled metastin in large excess is also provided. The reaction is carried out at approximately 0°C to 50°C, preferably 4°C to 37°C for 20 minutes to 24 hours, preferably 30 minutes to 3 hours. After completion of the reaction, the reaction mixture is filtrated through glass fiber filter paper, etc. and washed with an appropriate volume of the same buffer. The residual radioactivity on the glass fiber filter paper is then measured by means of a liquid scintillation counter or  $\gamma$ -counter. When nonspecific binding (NSB) is subtracted from the count (B0) where any antagonizing substance is absent and the resulting count (B0 minus NSB) is made 100%, the test compound showing the specific binding amount (B minus NSB) of, e.g., 50% or less may be selected as a candidate substance.

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